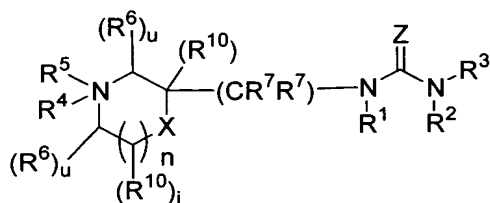


What is Claimed is:

1. A compound of formula (I):



5

or stereoisomers or pharmaceutically acceptable salts thereof, wherein:

10 Z is selected from O, S, N(R^d), C(CN)₂, CH(NO₂), and CH(CN);

X is C(R⁸)(R⁹);

15 R¹ and R² are independently selected from H, C₁₋₈ alkyl, C₂₋₈ alkenyl, and C₂₋₈ alkynyl;

R^d is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, CON(R^f)R^f, OR^e, CN, NO₂, and (CH₂)_r-phenyl substituted with 0-3 R¹⁸;

20

R^e, at each occurrence, is independently selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with 0-3 R¹⁸;

25 R^f, at each occurrence, is independently selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with 0-3 R¹⁸, or optionally, two R^f may be taken together with the nitrogen to which both are

attached to form a pyrrolidine, piperidine,
piperazine or morpholine ring;

R^3 is selected from a $(CR^{3'}R^{3'})_r-C_{3-6}$ carbocyclic residue
5 substituted with 0-5 R^{15} and a $(CR^{3'}R^{3'})_r-5-10$
membered heterocyclic system containing 1-4
heteroatoms selected from N, O, and S, substituted
with 0-3 R^{15} , with the proviso that the heterocyclic
residue is not cycloheptimidazolyl;

10

$R^{3'}$, at each occurrence, is independently selected from
H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^4 is absent, taken with the nitrogen to which it is
15 attached to form an N-oxide, or selected from C_{1-8}
alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$
cycloalkyl, $(CH_2)_qC(O)R^{4b}$, $(CH_2)_qC(O)NR^{4a}R^{4a}$,
 $(CH_2)_qC(O)OR^{4b}$, and a $(CH_2)_r-C_{3-6}$ carbocyclic residue
substituted with 0-3 R^{4C} ;

20

R^{4a} , at each occurrence, is independently selected from
H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

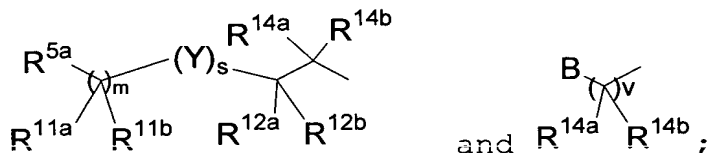
R^{4b} , at each occurrence, is independently selected from
25 C_{1-6} alkyl, C_{2-8} alkenyl, $(CH_2)_rC_{3-6}$ cycloalkyl, C_{2-8}
alkynyl, and phenyl;

R^{4C} , at each occurrence, is independently selected from
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6}
30 cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$,

$(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{SC}_{1-5}$ alkyl,
 $(\text{CH}_2)_r\text{NR}^{4a}\text{R}^{4a}$, and $(\text{CH}_2)_r\text{phenyl}$;

R^5 is selected from

5



Y is selected from O , $\text{N}(\text{R}^{25})$, S , $\text{S}(\text{O})$, and $\text{S}(\text{O})_2$;

- 10 ring B is a 5-7 membered cycloalkyl ring optionally
 containing a $\text{C}=\text{O}$, and being substituted with 0-2
 R^{11a} , wherein the cycloalkyl is fused with a benzo
 group substituted with 0-3 R^{16} or is fused with a 5-6
 membered aromatic heterocyclic ring having 0-3 N,
 15 0-1 O, or 0-1 S, the heterocyclic ring being
 substituted with 0-3 R^{16} ;

- alternatively, ring B is a fused 5-7 membered saturated
 heterocyclic ring containing 0-1 O, $\text{N}(\text{R}^{16})$, S, $\text{S}(\text{O})$,
 20 and $\text{S}(\text{O})_2$, substituted with 0-2 R^{11a} , the
 heterocyclic ring being fused with a benzo group
 substituted with 0-3 R^{16} or is fused with a 5-6
 membered heterocyclic ring having 0-3 N, 0-1 O, or
 0-1 S, the heterocyclic ring being substituted with
 25 0-3 R^{16} ;

provided that if ring B is a heterocyclic ring, then the
 number of carbon atoms separating the heteroatom of

ring B and the nitrogen atom of structure (I) bonded to R⁵ is at least 2;

R^{5a} is selected from a C₃₋₁₀ carbocyclic residue

5 substituted with 0-5 R¹⁶, and a 5-10 membered heterocyclic residue containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R¹⁶;

10 R⁶, at each occurrence, is independently selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, (CF₂)_rCF₃, CN, (CH₂)_rNR^{6a}R^{6a}, (CH₂)_qOH, (CH₂)_qOR^{6b}, (CH₂)_qSH, (CH₂)_qSR^{6b}, (CH₂)_rC(O)OH, (CH₂)_rC(O)R^{6b}, (CH₂)_rC(O)NR^{6a}R^{6a}, (CH₂)_qNR^{6d}C(O)R^{6a}, (CH₂)_rC(O)OR^{6b}, (CH₂)_qOC(O)R^{6b}, (CH₂)_rS(O)_pR^{6b},
15 (CH₂)_rS(O)₂NR^{6a}R^{6a}, (CH₂)_rNR^{6d}S(O)₂R^{6b}, and (CH₂)_tphenyl substituted with 0-3 R^{6c};

R^{6a}, at each occurrence, is independently selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl
20 substituted with 0-3 R^{6c};

R^{6b}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with 0-3 R^{6c};

25 R^{6c}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl, (CH₂)_rOH, (CH₂)_rSC₁₋₅ alkyl, and (CH₂)_rNR^{6d}R^{6d};

R^{6d} , at each occurrence, is independently selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

5 R^7 , at each occurrence, is independently selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_qOH$, $(CH_2)_qSH$, $(CH_2)_qOR^{7d}$, $(CH_2)_qSR^{7d}$, $(CH_2)_qNR^{7a}R^{7a}$, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{7b}$, $(CH_2)_rC(O)NR^{7a}R^{7a}$, $(CH_2)_qNR^{7a}C(O)R^{7a}$, $(CH_2)_qNR^{7a}C(O)H$, $(CH_2)_rC(O)OR^{7b}$,
 10 $(CH_2)_qOC(O)R^{7b}$, $(CH_2)_qS(O)_pR^{7b}$, $(CH_2)_qS(O)_2NR^{7a}R^{7a}$, $(CH_2)_qNR^{7a}S(O)_2R^{7b}$, C_{1-6} haloalkyl, a $(CH_2)_r-C_{3-6}$ carbocyclic residue substituted with 0-3 R^{7c} , and a $(CH_2)_r-5-10$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S,
 15 substituted with 0-2 R^{7c} ;

R^{7a} , at each occurrence, is independently selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, a $(CH_2)_r-C_{3-6}$ carbocyclic residue substituted with 0-5 R^{7e} ,
 20 and a $(CH_2)_r-5-10$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{7e} ;

R^{7b} , at each occurrence, is independently selected from
 25 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, a $(CH_2)_r-C_{3-6}$ carbocyclic residue substituted with 0-2 R^{7e} , and a $(CH_2)_r-5-6$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{7e} ;

R^{7c} , at each occurrence, is independently selected from
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$
cycloalkyl, Cl, Br, I, F, $(CF_2)_rCF_3$, NO_2 , CN,
5 $(CH_2)_rNR^{7f}R^{7f}$, $(CH_2)_rOH$, $(CH_2)_rOC_{1-4}$ alkyl, $(CH_2)_rSC_{1-4}$
alkyl, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{7b}$, $(CH_2)_rC(O)NR^{7f}R^{7f}$,
 $(CH_2)_rNR^{7f}C(O)R^{7a}$, $(CH_2)_rC(O)OC_{1-4}$ alkyl,
 $(CH_2)_rOC(O)R^{7b}$, $(CH_2)_rC(=NR^{7f})NR^{7f}R^{7f}$, $(CH_2)_rS(O)_pR^{7b}$,
 $(CH_2)_rNHC(=NR^{7f})NR^{7f}R^{7f}$, $(CH_2)_rS(O)_2NR^{7f}R^{7f}$,
10 $(CH_2)_rNR^{7f}S(O)_2R^{7b}$, and $(CH_2)_r$ phenyl substituted with
0-3 R^{7e} ;

R^{7d} , at each occurrence, is independently selected from
 C_{1-6} alkyl substituted with 0-3 R^{7e} , alkenyl,
15 alkynyl, and a C_{3-6} carbocyclic residue substituted
with 0-3 R^{7c} ;

R^{7e} , at each occurrence, is independently selected from
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6}
20 cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$,
 $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl,
 $(CH_2)_rNR^{7f}R^{7f}$, and $(CH_2)_r$ phenyl;

R^{7f} , at each occurrence, is independently selected from
25 H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^8 is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8}
alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CF_2)_rCF_3$,
 $(CH_2)_rN(R^{18a})R^{18b}$, $(CH_2)_rOH$, $(CH_2)_rOR^{19}$, $(CH_2)_rSH$,

$(\text{CH}_2)_r\text{SR}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{19}$, $(\text{CH}_2)_r\text{OC}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{S}(\text{O})_2\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$,
5 $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{R}^{19}$, a $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-C}_3\text{-10}$
carbocyclic residue substituted with 0-5 R^{17} , and a
 $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-5-10}$ membered heterocyclic system
containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-3 R^{17} ;

10

R^{8a} and R^{8b} , at each occurrence, are independently
selected from H, C_{1-6} alkyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl,
and $(\text{CH}_2)_r$ phenyl substituted with 0-3 R^{18} ;

15 R^9 is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8}
alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl, $(\text{CF}_2)_r\text{CF}_3$,
 $(\text{CH}_2)_q\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_q\text{OH}$, $(\text{CH}_2)_q\text{OR}^{19}$, $(\text{CH}_2)_q\text{SH}$,
 $(\text{CH}_2)_q\text{SR}^{19}$, $(\text{CH}_2)_q\text{C}(\text{O})\text{OH}$, $(\text{CH}_2)_q\text{C}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_q\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_q\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{R}^{19}$,
20 $(\text{CH}_2)_q\text{C}(\text{O})\text{OR}^{19}$, $(\text{CH}_2)_q\text{OC}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_q\text{S}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_q\text{S}(\text{O})_2\text{R}^{19}$, $(\text{CH}_2)_q\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_q\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{R}^{19}$, a $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-C}_3\text{-10}$
carbocyclic residue substituted with 0-5 R^{17} , and a
 $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-5-10}$ membered heterocyclic system
25 containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-3 R^{17} ;

alternatively, R^8 and R^9 taken together are selected from
 $=\text{O}$, $=\text{S}$, $=\text{NR}^{9a}$;

- R^{9a} is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r C_{3-6}$ cycloalkyl, $(CH_2)_r OH$, $(CH_2)_r OC_{1-6}$ alkyl, $(CH_2)_r C(O)R^{19}$, $(CH_2)_r C(O)N(R^{18a})R^{18b}$,
 5 $(CH_2)_r C(O)OR^{19}$, $(CH_2)_r S(O)_2R^{19}$,
 $(CH_2)_r S(O)_2N(R^{18a})R^{18b}$, and $(CH_2)_r$ phenyl substituted with 0-3 R^{17} ;
- R^{9b} , at each occurrence are independently selected from H,
 10 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r C_{3-6}$ cycloalkyl, $(CF_2)_r CF_3$, $(CH_2)_r N(R^{18a})R^{18b}$, $(CH_2)_r OH$,
 $(CH_2)_r OR^{19}$, $(CH_2)_r SH$, $(CH_2)_r SR^{19}$, $(CH_2)_r C(O)OH$,
 $(CH_2)_r C(O)R^{19}$, $(CH_2)_r C(O)N(R^{18a})R^{18b}$,
 $(CH_2)_r N(R^{18c})C(O)R^{19}$, $(CH_2)_r C(O)OR^{19}$, $(CH_2)_r OC(O)R^{19}$,
 15 $(CH_2)_r S(O)R^{19}$, $(CH_2)_r S(O)_2R^{19}$, $(CH_2)_r S(O)_2N(R^{18a})R^{18b}$,
 $(CH_2)_r N(R^{18c})S(O)_2R^{19}$, and $(CH_2)_r$ phenyl substituted with 0-3 R^{17} ;
- R^{10} , at each occurrence, is independently selected from H,
 20 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r C_{3-6}$ cycloalkyl, $(CF_2)_r CF_3$, CN, $(CH_2)_r NR^{10a}R^{10a}$, $(CH_2)_r OH$,
 $(CH_2)_r OR^{10b}$, $(CH_2)_r SH$, $(CH_2)_r SR^{10b}$, $(CH_2)_r C(O)OH$,
 $(CH_2)_r C(O)R^{10b}$, $(CH_2)_r C(O)NR^{10a}R^{10a}$,
 $(CH_2)_r NR^{10d}C(O)R^{10a}$, $(CH_2)_r C(O)OR^{10b}$, $(CH_2)_r OC(O)R^{10b}$,
 25 $(CH_2)_r S(O)_p R^{10b}$, $(CH_2)_r S(O)_2 NR^{10a}R^{10a}$,
 $(CH_2)_r NR^{10d}S(O)_2 R^{10b}$, and $(CH_2)_t$ phenyl substituted with 0-3 R^{10c} ;

R^{10a}, at each occurrence, is independently selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with 0-3 R^{10c};

5 R^{10b}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with 0-3 R^{10c};

10 R^{10c}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl, (CH₂)_rOH, (CH₂)_rSC₁₋₅ alkyl, and (CH₂)_rNR^{10d}R^{10d};

15 R^{10d}, at each occurrence, is independently selected from H, C₁₋₆ alkyl, and C₃₋₁₀ cycloalkyl;

R^{11a} and R^{12a}, at each occurrence are independently selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, (CF₂)_rCF₃,
 20 (CH₂)_rN(R^{18a})R^{18b}, (CH₂)_rOH, (CH₂)_rOR¹⁹, (CH₂)_rSH, (CH₂)_rSR¹⁹, (CH₂)_rC(O)OH, (CH₂)_rC(O)R¹⁹, (CH₂)_rC(O)N(R^{18a})R^{18b}, (CH₂)_rN(R^{18c})C(O)R¹⁹, (CH₂)_rC(O)OR¹⁹, (CH₂)_rOC(O)R¹⁹, (CH₂)_rS(O)R¹⁹, (CH₂)_rS(O)₂R¹⁹, (CH₂)_rS(O)₂N(R^{18a})R^{18b},
 25 (CH₂)_rN(R^{18c})S(O)₂R¹⁹, and (CH₂)_rphenyl substituted with 0-3 R¹⁸;

R^{11b}, R^{12b}, R^{14a} and R^{14b} at each occurrence are independently selected from H, C₁₋₆ alkyl, C₂₋₈

- alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl,
 (CF₂)_rCF₃, (CH₂)_qN(R^{18a})R^{18b}, (CH₂)_qOH, (CH₂)_qOR¹⁹,
 (CH₂)_qSH, (CH₂)_qSR¹⁹, (CH₂)_rC(O)OH, (CH₂)_rC(O)R¹⁹,
 (CH₂)_rC(O)N(R^{18a})R^{18b}, (CH₂)_qN(R^{18c})C(O)R¹⁹,
 5 (CH₂)_rC(O)OR¹⁹, (CH₂)_qOC(O)R¹⁹, (CH₂)_qS(O)R¹⁹,
 (CH₂)_qS(O)₂R¹⁹, (CH₂)_qS(O)₂N(R^{18a})R^{18b},
 (CH₂)_qN(R^{18c})S(O)₂R¹⁹, and (CH₂)_rphenyl substituted
 with 0-3 R¹⁸;
- 10 alternatively, R^{11a} and R^{11b} taken together are selected
 form =O, or =NOH, or alternatively, R^{12a} and R^{12b}
 taken together are selected form =O, or =NOH;
- R¹⁵, at each occurrence, is independently selected from
 15 C₁₋₈ alkyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, Br, I, F, NO₂,
 CN, (CHR')_rNR^{15a}R^{15a}, (CHR')_rOH, (CHR')_rO(CHR')_rR^{15d},
 (CHR')_rSH, (CHR')_rC(O)H, (CHR')_rS(CHR')_rR^{15d},
 (CHR')_rC(O)OH, (CHR')_rC(O)(CHR')_rR^{15b},
 (CHR')_rC(O)NR^{15a}R^{15a}, (CHR')_rNR^{15f}C(O)(CHR')_rR^{15b},
 20 (CHR')_rNR^{15f}C(O)NR^{15f}R^{15f}, (CHR')_rC(O)O(CHR')_rR^{15d},
 (CHR')_rOC(O)(CHR')_rR^{15b}, (CHR')_rC(=NR^{15f})NR^{15a}R^{15a},
 (CHR')_rNHC(=NR^{15f})NR^{15f}R^{15f}, (CHR')_rS(O)_p(CHR')_rR^{15b},
 (CHR')_rS(O)₂NR^{15a}R^{15a}, (CHR')_rNR^{15f}S(O)₂(CHR')_rR^{15b},
 C₁₋₆ haloalkyl, C₂₋₈ alkenyl substituted with 0-3 R',
 25 C₂₋₈ alkynyl substituted with 0-3 R', (CHR')_rphenyl
 substituted with 0-3 R^{15e}, and a (CH₂)_r-5-10 membered
 heterocyclic system containing 1-4 heteroatoms
 selected from N, O, and S, substituted with 0-2 R^{15e};

R', at each occurrence, is independently selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, and (CH₂)_rphenyl substituted with R^{15e};

5

R^{15a}, at each occurrence, are selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-5 R^{15e}, and a (CH₂)_r-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

10

R^{15b}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-3 R^{15e}, and (CH₂)_r-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

15

R^{15d}, at each occurrence, is independently selected from C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₆ alkyl substituted with 0-3 R^{15e}, a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-3 R^{15e}, and a (CH₂)_r-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15e};

20

25

R^{15e}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃,

$(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, OH, SH, $(\text{CH}_2)_r\text{SC}_{1-5}$ alkyl,
 $(\text{CH}_2)_r\text{NR}^{15f}\text{R}^{15f}$, and $(\text{CH}_2)_r\text{phenyl}$;

R^{15f} , at each occurrence, is independently selected from
 5 H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{16} , at each occurrence, is independently selected from
 C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$
 cycloalkyl, Cl, Br, I, F, NO_2 , CN, $(\text{CHR}')_r\text{NR}^{16a}\text{R}^{16a}$,
 10 $(\text{CHR}')_r\text{OH}$, $(\text{CHR}')_r\text{O}(\text{CHR}')_r\text{R}^{16d}$, $(\text{CHR}')_r\text{SH}$,
 $(\text{CHR}')_r\text{C}(\text{O})\text{H}$, $(\text{CHR}')_r\text{S}(\text{CHR}')_r\text{R}^{16d}$, $(\text{CHR}')_r\text{C}(\text{O})\text{OH}$,
 $(\text{CHR}')_r\text{C}(\text{O})(\text{CHR}')_r\text{R}^{16b}$, $(\text{CHR}')_r\text{C}(\text{O})\text{NR}^{16a}\text{R}^{16a}$,
 $(\text{CHR}')_r\text{NR}^{16f}\text{C}(\text{O})(\text{CHR}')_r\text{R}^{16b}$, $(\text{CHR}')_r\text{C}(\text{O})\text{O}(\text{CHR}')_r\text{R}^{16d}$,
 $(\text{CHR}')_r\text{OC}(\text{O})(\text{CHR}')_r\text{R}^{16b}$, $(\text{CHR}')_r\text{C}(=\text{NR}^{16f})\text{NR}^{16a}\text{R}^{16a}$,
 15 $(\text{CHR}')_r\text{NHC}(=\text{NR}^{16f})\text{NR}^{16f}\text{R}^{16f}$, $(\text{CHR}')_r\text{S}(\text{O})_p(\text{CHR}')_r\text{R}^{16b}$,
 $(\text{CHR}')_r\text{S}(\text{O})_2\text{NR}^{16a}\text{R}^{16a}$, $(\text{CHR}')_r\text{NR}^{16f}\text{S}(\text{O})_2(\text{CHR}')_r\text{R}^{16b}$,
 C_{1-6} haloalkyl, C_{2-8} alkenyl substituted with 0-3 R' ,
 C_{2-8} alkynyl substituted with 0-3 R' , and
 $(\text{CHR}')_r\text{phenyl}$ substituted with 0-3 R^{16e} ;

20

R^{16a} , at each occurrence, is independently selected from
H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, a $(\text{CH}_2)_r$ -
 C_{3-6} carbocyclic residue substituted with 0-5 R^{16e} ,
and a $(\text{CH}_2)_r$ -5-10 membered heterocyclic system
 25 containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-2 R^{16e} ;

R^{16b}, at each occurrence, is independently selected from
 C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, a (CH₂)_rC₃₋₆
 carbocyclic residue substituted with 0-3 R^{16e}, and a
 (CH₂)_r-5-6 membered heterocyclic system containing
 5 1-4 heteroatoms selected from N, O, and S,
 substituted with 0-2 R^{16e};

R^{16d}, at each occurrence, is independently selected from
 C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₆ alkyl substituted
 10 with 0-3 R^{16e}, a (CH₂)_r-C₃₋₆ carbocyclic residue
 substituted with 0-3 R^{16e}, and a (CH₂)_r-5-6 membered
 heterocyclic system containing 1-4 heteroatoms
 selected from N, O, and S, substituted with 0-3 R^{16e};

15 R^{16e}, at each occurrence, is independently selected from
 C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆
 cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃,
 (CH₂)_rOC₁₋₅ alkyl, OH, SH, (CH₂)_rSC₁₋₅ alkyl,
 (CH₂)_rNR^{16f}R^{16f}, and (CH₂)_rphenyl;

20

R^{16f}, at each occurrence, is independently selected from
 H, C₁₋₅ alkyl, and C₃₋₆ cycloalkyl, and phenyl;

25 R¹⁷ at each occurrence is independently selected from =O,
 C₁₋₆ alkyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, F, Br, I, CN,
 NO₂, (CH₂)_rOR¹⁹, (CH₂)_rOH, (CH₂)_rSR¹⁹, (CH₂)_rS(O)R¹⁹,
 (CH₂)_rS(O)₂R¹⁹, (CH₂)_rS(O)₂N(R^{18a})R^{18b},
 (CH₂)_rN(R^{18c})C(O)R¹⁹ (CH₂)_rN(R^{18c})S(O)₂R¹⁹,
 (CH₂)_rC(O)OH, (CH₂)_rC(O)OR¹⁹, (CH₂)_rC(O)N(R^{18a})R^{18b},

- $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{OR}^{19}$,
 $(\text{CH}_2)_r\text{OC}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{N}(\text{R}^{18a})\text{R}^{18b}$, C_{1-6}
haloalkyl, C_{2-8} alkenyl substituted with 0-3 R^{17a} , C_{2-8}
alkynyl substituted with 0-3 R^{17a} , $(\text{CH}(\text{R}^{17a}))_r$ phenyl
5 substituted with 1-3 R^{18} , and $(\text{CH}(\text{R}^{17a}))_{r-5-10}$
membered heterocyclic system containing 1-4
heteroatoms selected from N, O, and S, substituted
with 0-2 R^{18} ;
- 10 R^{17a} at each occurrence is independently selected from H,
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$
cycloalkyl, and $(\text{CH}_2)_r$ phenyl substituted with 0-3
 R^{18} ;
- 15 R^{18} at each occurrence is independently selected from C_{1-6}
alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 ,
 $(\text{CF}_2)_r\text{CF}_3$, $(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{SC}_{1-5}$
alkyl, $(\text{CH}_2)_r\text{S}(\text{O})\text{C}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{S}(\text{O})_2\text{C}_{1-5}$ alkyl,
 $(\text{CH}_2)_r\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{C}_{1-5}$ alkyl
20 $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{C}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{C}(\text{O})\text{C}_{1-5}$ alkyl, and
 $(\text{CH}_2)_r\text{N}(\text{R}^{18a})\text{R}^{18b}$;
- 25 R^{18a} , R^{18b} , and R^{18c} at each occurrence are independently
selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;
- R^{19} at each occurrence is independently selected from C_{1-6}
alkyl, C_{3-6} cycloalkyl, and phenyl substituted with
0-3 R^{18} ;

alternatively, R^{18a} and R^{18b} along with the nitrogen to
 which both are attached form a pyrrolidine,
 piperidine, piperazine or morpholine ring;

5

R^{25} at each occurrence is independently selected from H,
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r C_{3-6}$
 cycloalkyl, $(CH_2)_r C(O)R^{19}$, $(CH_2)_r C(O)N(R^{18a})R^{18b}$,
 $(CH_2)_r C(O)OR^{19}$, $(CH_2)_r S(O)_2R^{19}$,
 10 $(CH_2)_r S(O)_2N(R^{18a})R^{18b}$, and $(CH_2)_r$ phenyl substituted
 with 0-3 R^{17} ;

i is selected from 0, 1, and 2;

15 m is selected from 0, 1, and 2;

s is selected from 0 and 1;

with the proviso: $m + s$ is selected from 0, 1, and 2;

20

n is selected from 1 and 2;

v is selected from 0, 1, 2, and 3;

25 with the proviso: that the total number of atoms between
 the nitrogen of which R' is attached and the fused
 ring B is less than or equal to 4;

r is selected from 0, 1, 2, 3, 4, and 5;

30

t is selected from 0, 1, 2, 3, 4, and 5;

q is selected from 1, 2, 3, 4, and 5;

p is selected from 1, 2, and 3;

5 u is selected from 0, 1 and, 2.

2. The compound of claim 1, wherein

10 R^{11a} and R^{12a}, at each occurrence are independently selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, (CF₂)_rCF₃, (CH₂)_rN(R^{18a})R^{18b}, (CH₂)_rOH, (CH₂)_rOR¹⁹, (CH₂)_rSH, (CH₂)_rSR¹⁹, (CH₂)_rC(O)OH, (CH₂)_rC(O)R¹⁹, (CH₂)_rC(O)N(R^{18a})R^{18b}, (CH₂)_rN(R^{18c})C(O)R¹⁹,
15 (CH₂)_rC(O)OR¹⁹, (CH₂)_rOC(O)R¹⁹, (CH₂)_rS(O)R¹⁹, (CH₂)_rS(O)₂R¹⁹, (CH₂)_rS(O)₂N(R^{18a})R^{18b}, (CH₂)_rN(R^{18c})S(O)₂R¹⁹, and (CH₂)_rphenyl substituted with 0-3 R¹⁸; and

20 R^{11b}, R^{12b}, R^{14a} and R^{14b} at each occurrence are independently selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, (CF₂)_rCF₃, (CH₂)_qN(R^{18a})R^{18b}, (CH₂)_qOH, (CH₂)_qOR¹⁹, (CH₂)_qSH, (CH₂)_qSR¹⁹, (CH₂)_rC(O)OH, (CH₂)_rC(O)R¹⁹,
25 (CH₂)_rC(O)N(R^{18a})R^{18b}, (CH₂)_qN(R^{18c})C(O)R¹⁹, (CH₂)_rC(O)OR¹⁹, (CH₂)_qOC(O)R¹⁹, (CH₂)_qS(O)R¹⁹, (CH₂)_qS(O)₂R¹⁹, (CH₂)_qS(O)₂N(R^{18a})R^{18b}, (CH₂)_qN(R^{18c})S(O)₂R¹⁹, and (CH₂)_rphenyl substituted with 0-3 R¹⁸.

30

3. The compound of claim 2, wherein

R¹ and R² are independently selected from H, and C₁₋₈ alkyl;

5

R⁴ is absent, taken with the nitrogen to which it is attached to form an N-oxide, or selected from C₁₋₈ alkyl, (CH₂)_rC₃₋₆ cycloalkyl, and a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-3 R^{4C}; and

10

R^{4C}, at each occurrence, is independently selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl, (CH₂)_rOH, (CH₂)_rSC₁₋₅ alkyl, (CH₂)_rNR^{4a}R^{4a}, and (CH₂)_rphenyl.

15

4. The compound of claim 3, wherein

Z is selected from O and S;

20

R⁶, at each occurrence, is independently selected from C₁₋₄ alkyl, (CH₂)_rC₃₋₆ cycloalkyl, (CH₂)_qNR^{6a}R^{6a}, (CH₂)_qOH, (CH₂)_qOR^{6b}, (CH₂)_rC(O)OH, (CH₂)_rC(O)R^{6b}, (CH₂)_rC(O)NR^{6a}R^{6a}, (CH₂)_qNR^{6d}C(O)R^{6a}, (CH₂)_rS(O)₂NR^{6a}R^{6a}, (CH₂)_rNR^{6d}S(O)₂R^{6b}, and (CH₂)_tphenyl substituted with 0-3 R^{6C};

25

R^{6a} and R^{6a}, at each occurrence, are selected from H, methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclopentyl, cyclohexyl, and phenyl;

30

R^{6b} , at each occurrence, is independently selected from methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclopentyl, cyclohexyl, and phenyl;

5

R^{6c} , at each occurrence, is independently selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{6d}R^{6d}$;

10

R^{6d} , at each occurrence, is independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclopentyl, and cyclohexyl;

15 R^7 , is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_qOH$, $(CH_2)_qOR^{7d}$, $(CH_2)_qNR^{7a}R^{7a}$, $(CH_2)_rC(O)R^{7b}$, $(CH_2)_rC(O)NR^{7a}R^{7a}$, $(CH_2)_qNR^{7a}C(O)R^{7a}$, $(CH_2)_qNR^{7a}C(O)H$, $(CH_2)_rC(O)OR^{7b}$, $(CH_2)_qOC(O)R^{7b}$, C_{1-6} haloalkyl, a $(CH_2)_r-C_{3-6}$ carbocyclic residue
 20 substituted with 0-3 R^{7c} , and a $(CH_2)_r-5-10$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{7c} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl,
 25 benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, indazolyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-
 30 triazolyl, 1,2,3-triazolyl, tetrazolyl,

thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl;

5 R^{7a} , at each occurrence, is independently selected from H, C_{1-6} alkyl, and a $(CH_2)_r-C_{3-6}$ carbocyclic residue substituted with 0-5 R^{7e} ;

10 R^{7b} , at each occurrence, is independently selected from C_{1-6} alkyl, a $(CH_2)_r-C_{3-6}$ carbocyclic residue substituted with 0-2 R^{7e} ;

15 R^{7c} , at each occurrence, is independently selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, $(CF_2)_rCF_3$, NO_2 , CN, $(CH_2)_rNR^{7f}R^{7f}$, $(CH_2)_rOH$, $(CH_2)_rOC_{1-4}$ alkyl, $(CH_2)_rSC_{1-4}$ alkyl, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{7b}$, $(CH_2)_rC(O)NR^{7f}R^{7f}$, $(CH_2)_rNR^{7f}C(O)R^{7a}$, $(CH_2)_rC(O)OC_{1-4}$ alkyl, $(CH_2)_rOC(O)R^{7b}$, $(CH_2)_rC(=NR^{7f})NR^{7f}R^{7f}$, $(CH_2)_rS(O)_pR^{7b}$, $(CH_2)_rNHC(=NR^{7f})NR^{7f}R^{7f}$, $(CH_2)_rS(O)_2NR^{7f}R^{7f}$,
20 $(CH_2)_rNR^{7f}S(O)_2R^{7b}$, and $(CH_2)_r$ phenyl substituted with 0-3 R^{7e} ;

25 R^{7d} , at each occurrence, is independently selected from C_{1-6} alkyl substituted with 0-3 R^{7e} , and a C_{3-6} carbocyclic residue substituted with 0-3 R^{7c} ;

R^{7e} , at each occurrence, is independently selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$,

$(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, OH, SH, $(\text{CH}_2)_r\text{SC}_{1-5}$ alkyl,
 $(\text{CH}_2)_r\text{NR}^{7f}\text{R}^{7f}$, and $(\text{CH}_2)_r\text{phenyl}$;

5 R^{7f} , at each occurrence, is independently selected from
 H, methyl, ethyl, propyl, i-propyl, butyl,
 cyclopropyl, cyclopentyl and cyclohexyl;

R^{10} , at each occurrence, is independently selected from H,
 C_{1-4} alkyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl, $(\text{CH}_2)_r\text{NR}^{10a}\text{R}^{10a}$,
 10 $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{OR}^{10b}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{10b}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^{10a}\text{R}^{10a}$, $(\text{CH}_2)_r\text{NR}^{10d}\text{C}(\text{O})\text{R}^{10a}$,
 $(\text{CH}_2)_r\text{S}(\text{O})_2\text{NR}^{10a}\text{R}^{10a}$, $(\text{CH}_2)_r\text{NR}^{10d}\text{S}(\text{O})_2\text{R}^{10b}$, and
 $(\text{CH}_2)_t\text{phenyl}$ substituted with 0-3 R^{10c} ;

15 R^{10a} and R^{10a} , at each occurrence, are selected from H,
 methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl,
 cyclopentyl, cyclohexyl, and phenyl;

R^{10b} , at each occurrence, is independently selected from
 20 methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl,
 cyclopentyl, cyclohexyl, and phenyl;

R^{10c} , at each occurrence, is independently selected from
 C_{1-10} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 ,
 25 $(\text{CF}_2)_r\text{CF}_3$, $(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{SC}_{1-5}$
 alkyl, and $(\text{CH}_2)_r\text{NR}^{10d}\text{R}^{10d}$; and

R^{10d} , at each occurrence, is independently selected from
 H, methyl, ethyl, propyl, i-propyl, butyl,
 30 cyclopropyl, cyclopentyl, and cyclohexyl.

5. The compound of claim 4, wherein

R^3 is selected from a $(CR^{3'}H)_r$ - C_{3-8} carbocyclic residue

5 substituted with 0-5 R^{15} , wherein the carbocyclic residue is selected from phenyl, naphthyl, and adamantyl; and a $(CR^{3'}H)_r$ -heterocyclic system substituted with 0-3 R^{15} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl,
 10 furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, indazolyl, isoindolyl, isothiadiazolyl, isoxazolyl,
 15 piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^{5a} is selected from phenyl substituted with 0-5 R^{16} ; and

20 a heterocyclic residue substituted with 0-3 R^{16} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl,
 25 quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl;

30

R^8 is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CF_2)_rCF_3$,

$(\text{CH}_2)_r\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{OR}^{19}$, $(\text{CH}_2)_r\text{SH}$,
 $(\text{CH}_2)_r\text{SR}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{19}$, $(\text{CH}_2)_r\text{OC}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})\text{R}^{19}$,
5 $(\text{CH}_2)_r\text{S}(\text{O})_2\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{R}^{19}$, a $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-C}_3\text{-10}$
carbocyclic residue substituted with 0-5 R^{17} , and a
 $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-5-10}$ membered heterocyclic system
containing 1-4 heteroatoms selected from N, O, and
10 S, substituted with 0-3 R^{17} , wherein the heterocyclic
system is selected from pyridinyl, thiophenyl,
furanlyl, indazolyl, benzothiazolyl, benzimidazolyl,
benzothiophenyl, benzofuranlyl, benzoxazolyl,
15 benzisoxazolyl, quinolinyl, isoquinolinyl,
imidazolyl, indolyl, indolinyl, isoindolyl,
isothiadiazolyl, isoxazolyl, piperidinyl,
pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl,
tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl,
pyrazinyl, and pyrimidinyl;
20 R^{8a} and R^{8b} , at each occurrence, are independently
selected from H, methyl, ethyl, propyl, i-propyl,
butyl, cyclopropyl, cyclopentyl, cyclohexyl, and
 $(\text{CH}_2)_r$ phenyl substituted with 0-3 R^{18} ;
25 R^9 is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8}
alkynyl, $(\text{CH}_2)_r\text{C}_3\text{-6}$ cycloalkyl, $(\text{CF}_2)_r\text{CF}_3$,
 $(\text{CH}_2)_q\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_q\text{OH}$, $(\text{CH}_2)_q\text{OR}^{19}$, $(\text{CH}_2)_q\text{SH}$,
 $(\text{CH}_2)_q\text{SR}^{19}$, $(\text{CH}_2)_q\text{C}(\text{O})\text{OH}$, $(\text{CH}_2)_q\text{C}(\text{O})\text{R}^{19}$,
30 $(\text{CH}_2)_q\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_q\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{R}^{19}$,

$(\text{CH}_2)_q\text{C}(\text{O})\text{OR}^{19}$, $(\text{CH}_2)_q\text{OC}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_q\text{S}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_q\text{S}(\text{O})_2\text{R}^{19}$, $(\text{CH}_2)_q\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_q\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{R}^{19}$, a $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-C}_{3-10}$
carbocyclic residue substituted with 0-5 R^{17} , and a
5 $(\text{C}(\text{R}^{8a})(\text{R}^{8b}))_r\text{-5-10}$ membered heterocyclic system
containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-3 R^{17} , wherein the heterocyclic
system is selected from pyridinyl, thiophenyl,
furanyl, indazolyl, benzothiazolyl, benzimidazolyl,
10 benzothiophenyl, benzofuranyl, benzoxazolyl,
benzisoxazolyl, quinolinyl, isoquinolinyl,
imidazolyl, indolyl, indolinyl, isoindolyl,
isothiadiazolyl, isoxazolyl, piperidinyl,
pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl,
15 tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl,
pyrazinyl, and pyrimidinyl;

alternatively, R^8 and R^9 taken together are selected from
 $=\text{O}$, $=\text{S}$, $=\text{NR}^{9a}$;

20 R^{9a} is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8}
alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{OC}_{1-6}$
alkyl, $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{19}$, and $(\text{CH}_2)_r\text{phenyl}$ substituted with 0-3
25 R^{17} ; and

R^{9b} , at each occurrence are independently selected from H,
 C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$
cycloalkyl, $(\text{CF}_2)_r\text{CF}_3$, $(\text{CH}_2)_r\text{N}(\text{R}^{18a})\text{R}^{18b}$, $(\text{CH}_2)_r\text{OH}$,
30 $(\text{CH}_2)_r\text{OR}^{19}$, $(\text{CH}_2)_r\text{SH}$, $(\text{CH}_2)_r\text{SR}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$,

$(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{C}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{19}$, $(\text{CH}_2)_r\text{OC}(\text{O})\text{R}^{19}$,
 $(\text{CH}_2)_r\text{S}(\text{O})\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})_2\text{R}^{19}$, $(\text{CH}_2)_r\text{S}(\text{O})_2\text{N}(\text{R}^{18a})\text{R}^{18b}$,
 $(\text{CH}_2)_r\text{N}(\text{R}^{18c})\text{S}(\text{O})_2\text{R}^{19}$, and $(\text{CH}_2)_r\text{phenyl}$ substituted
 5 with 0-3 R^{17} .

6. The compound of claim 5, wherein

10 R^1 and R^2 are H;

R^{5a} is phenyl substituted with 1-3 R^{16} ;

R^{16} , at each occurrence, is independently selected from
 C_{1-8} alkyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl, CF_3 , Cl, Br, I, F,
 15 $\text{NR}^{16a}\text{R}^{16a}$, NO_2 , CN, OH, OR^{16d} , $\text{C}(\text{O})\text{R}^{16b}$, $\text{C}(\text{O})\text{NR}^{16a}\text{R}^{16a}$,
 and $\text{NR}^{16f}\text{C}(\text{O})\text{R}^{16b}$;

R^{16a} , at each occurrence, is independently selected from
 H, methyl, ethyl, propyl, i-propyl, butyl,
 20 cyclopropyl, cyclopentyl, cyclohexyl, and
 $(\text{CH}_2)_r\text{phenyl}$ substituted with 0-3 R^{16e} ;

R^{16b} , at each occurrence, is independently selected from
 methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl,
 25 cyclopentyl, cyclohexyl, and $(\text{CH}_2)_r\text{phenyl}$ substituted
 with 0-3 R^{16e} ;

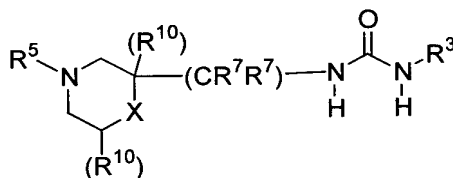
R^{16d} , at each occurrence, is independently selected from
 methyl, ethyl, propyl, i-propyl, butyl, and phenyl;
 30

R^{16e} , at each occurrence, is independently selected from methyl, ethyl, propyl, i-propyl, butyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

5 R^{16f} , at each occurrence, is independently selected from H, methyl, ethyl, propyl, i-propyl, and butyl.

7. The compound of claim 6, wherein the compound is of formula (I-i)

10



(I-i);

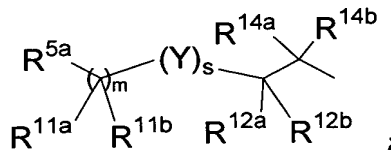
R^{10} is selected from H, methyl, ethyl, propyl, i-propyl, butyl, OH, and OR^{10b} ; and

15

R^{10b} is selected from methyl, ethyl, propyl, i-propyl, and butyl.

8. The compound of claim 7, wherein

20 R^5 is



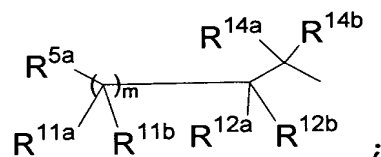
25 R^{11a} and R^{12a} , at each occurrence are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, pentyl, hexyl, cyclopropyl, cyclopentyl, cyclohexyl, CF_3 , $(CH_2)_rN(R^{18a})R^{18b}$, $(CH_2)_rOH$;

R^{11b}, R^{12b}, R^{14a} and R^{14b} at each occurrence are
independently selected from H, methyl, ethyl,
propyl, i-propyl, butyl, pentyl, hexyl, cyclopropyl,
5 cyclopentyl, cyclohexyl, CF₃, (CH₂)_rN(R^{18a})R^{18b},
(CH₂)_rOH;

R²⁵ at each occurrence is independently selected from H,
methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl,
10 cyclopentyl, cyclohexyl, (CH₂)_rC(O)R¹⁹,
(CH₂)_rC(O)N(R^{18a})R^{18b}, (CH₂)_rC(O)OR¹⁹, and (CH₂)_rphenyl
substituted with 0-3 R¹⁷.

9. The compound of claim 8, wherein
15

R⁵ is



20 R⁷, at each occurrence, is selected from H, methyl,
ethyl, propyl, i-propyl, butyl, (CH₂)_qOH;

R^{11a} and R^{12a}, at each occurrence, are independently
selected from H, methyl, and ethyl;

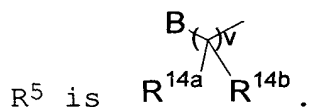
25

R^{11b}, R^{12b}, R^{14a}, and R^{14b}, at each occurrence, are
independently selected from H, methyl, ethyl and OH;
and

R16, at each occurrence, is independently selected from methyl, Cl, F, CF₃, and CN.

10. The compound of claim 7, wherein

5



11. The compound of claim 9, wherein R⁸ and R⁹ do not both equal H.

10

12. The compound of claim 1, wherein the compound is selected from the compounds of Table 1 or

15 1-{1-[3-(4-fluorophenyl)-2,2-dimethylpropyl]-piperidin-3-ylmethyl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{1-[3-(4-fluorophenyl)-propyl]-piperidin-3-ylmethyl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

20

1-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{1-[2-(4-trifluoromethylphenyl)-ethyl]-piperidin-3-ylmethyl}-urea;

25 1-(5-acetyl-4-methylthiazol-2-yl)-3-{1-[2-(4-fluorophenyl)ethyl]-piperidin-3-ylmethyl}urea;

1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)phenyl]-3-{trans-1-[2-(4-fluorophenyl)-ethyl]-4-methylpiperidin-3-ylmethyl}-urea;

30

- 1-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-3-{cis-1-[2-(4-fluorophenyl)-ethyl]-4-methylpiperidin-3-ylmethyl}-urea;
- 5 trans-1-{4-(benzyl-methylamino)-1-[2-(4-fluorophenyl)-ethyl]-piperidin-3-ylmethyl}-3-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;
- trans-1-{4-methylamino-1-[2-(4-fluorophenyl)-ethyl]-piperidin-3-ylmethyl}-3-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;
- 10 trans-N-{3-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureidomethyl}-1-[3-(4-fluoro-phenyl)-propyl]-piperidin-4-yl}-N-methyl-acetamide;
- 15 trans-N-{3-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureidomethyl}-1-[3-(4-fluoro-phenyl)-propyl]-piperidin-4-yl}-N-methyl-methanesulfonamide;
- 20 (S)-1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{1-[2-(4-fluorophenyl)-2-oxo-ethyl]-piperidin-3-ylmethyl}-urea;
- 25 (S)-1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{1-[2-(4-fluorophenyl)-2-hydroxyimino-ethyl]-piperidin-3-ylmethyl}-urea;
- 1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{1-[2-(4-fluorophenyl)-2-(RS)-hydroxyethyl]- (S)-piperidin-3-ylmethyl}-urea;
- 30

(S)-1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{1-[2-(4-fluorophenyl)-ethyl]-piperidin-3-ylmethyl}-urea;

5 1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)phenyl]-3-{1-[2-(4-fluorophenyl)-ethyl]-4-ethylpiperidin-3-ylmethyl}-urea; and

10 1-[3-ethyl-5-(1-methyl-1H-tetrazol-5-yl)phenyl]-3-{1-[2-(4-fluorophenyl)-ethyl]-4,4-dimethylpiperidin-3-ylmethyl}-urea.

13. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1.

14. A method for modulation of chemokine receptor activity comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1.

15. A method for treating asthma, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically

effective amount of a compound according to Claim 16, or a pharmaceutically acceptable salt thereof.

18. The method of claim 17 wherein modulation of
5 chemokine receptor activity comprises contacting a CCR3 receptor with an effective inhibitory amount of the compound.

19. A method for treating inflammatory disorders
10 comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

15 20. A method according to Claim 19, wherein the disorder is selected from asthma, allergic rhinitis, atopic dermatitis, inflammatory bowel diseases, idiopathic pulmonary fibrosis, bullous pemphigoid, helminthic parasitic infections, allergic colitis,
20 eczema, conjunctivitis, transplantation, familial eosinophilia, eosinophilic cellulitis, eosinophilic pneumonias, eosinophilic fasciitis, eosinophilic gastroenteritis, drug induced eosinophilia, HIV infection, cystic fibrosis, Churg-Strauss syndrome,
25 lymphoma, Hodgkin's disease, and colonic carcinoma.

21. The method according to Claim 20, wherein the disorder is selected from asthma, allergic rhinitis, atopic dermatitis, and inflammatory bowel diseases.

30

22. The method according to Claim 21, wherein the disorder is asthma.